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EXAMINER
JONES, DWAYNE C

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/678,591	Applicant(s) QUAY, STEVEN C.	
	Examin r Dwayne C Jones	Art Unit 1614	

-- The MAILING DATE f this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *17 October 2002* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Claims

1. Claims 1-50 are pending.

2. Claims 1-50 are rejected.

Response to Arguments

3. Applicant's arguments filed October 17, 2002 have been fully considered but they are not persuasive with respect to all of the alleged arguments. Applicant's attorney argues the following points. Each set of arguments will be grouped under the corresponding rejection of record. Applicant alleges that the rejection under 35 U.S.C. 112, first paragraph is unfounded. First, appellant argues that the instant invention does provide an enabling disclosure for the prevention or prophylaxis of breast cancer. Second, applicant argues that any such evidence that is not supported by documentation but is founded within the examiner's personal knowledge must be articulated in the appropriate context and form, in compliance with 37 CFR 1.1707(b). Applicant next argues over the rejection of claims 1-12, 26-33 and 39-50 under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Cassoni et al. For this rejection, applicant argues that Cassoni et al. reports that there is no significant effect of oxytocin on the proliferation rate of MCF7 cells was observed. In addition, applicant appellant alleges that Cassoni et al. emphasizes that Taylor et al. found enhancement of the growth rate of MCF7 cells as a result of the administration of oxytocin. Next, applicant alleges that the rejection under 35 U.S.C.

103(a) as being unpatentable over Harris et al. in view of Boer et al. and further in view of Leckman et al. Accordingly, this rejection was modified to reject claims 13-25 and 34-38 under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Leckman et al. Applicant also argues that in the rejection of claims 26-37 under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931, the prior art reference of Harris et al. fails to teach or suggest the efficacy of carbetocin or another oxytocin analog for prophylaxis or treatment of breast cancer or a psychiatric disorder in a mammalian patient. Appellant first argues that the instant invention does provide an enabling disclosure for the prevention or prophylaxis of breast cancer. In fact, appellant states that the in vivo animal model assays for assessing the operability of the invention provide support for the prevention or prophylaxis of breast cancer. This information provides enablement for the treatment of breast cancer and the prevention or prophylaxis of breast cancer in the mammal of rats. However, the prior art reference of Stein et al. clearly teach one skilled in the art that cancer therapy remains highly unpredictable, and no example exists for efficacy of a single product against tumors generally.

4. Second, applicant argues that any such evidence that is not supported by documentation but is founded within the examiner's personal knowledge must be articulated in the appropriate context and form, in compliance with 37 CFR 1.1707(b). In addition, applicant alleges that the Office has a burden of establishing sufficient factual evidence that is "inconsistent" with the assertions made by applicant, and which prima facie demonstrates that the contested claims are not enabled. The factual

evidence provided by the Office, which demonstrates to applicant that cancer therapy is not only highly unpredictable but that there is no one example existing for efficacy of a single product against tumors generally, (as cited from the Stein reference). Accordingly, this evidence specifically teaches that cancer therapy is highly unpredictable. In addition, the prior art reference of Sapino et al. states that oxytocin receptors are found in normal breast tissue and in benign and malignant breast lesions. Sapino et al. further teach that although the oxytocin receptors are widely expressed, their biological and clinical significance remains to be determined, (see column 2, page 2186).

5. Regarding the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Harris et al. in view of Cassoni et al., applicant argues that Cassoni et al. reports that there is no significant effect of oxytocin on the proliferation rate of MCF7 cells was observed. This allegation is found unpersuasive for the following reasons. Figure D states that 17-beta-oestradiol enhances the T47D cell proliferation at both 96 and 144 hours out vs. control rather than the alleged no significant effect. In addition, Figure D specifically teaches that when oxytocin is added there is significant reduction of the effects of 17-beta-oestradiol.

6. In addition, applicant appellant alleges that Cassoni et al. emphasizes that Taylor et al. found enhancement of the growth rate of MCF7 cells as a result of the administration of oxytocin. Foremost, the prior art reference of Taylor et al. was not utilized in the Office action of June 17, 2002 and is therefore irrelevant. However, Cassoni et al. do in fact speculate about the results obtained from Taylor et al. in that

these results could have used a higher concentration of oxytocin because there was different oestrogen content in the culture medium, (see column 2, 1st paragraph, page 471). The fact remains that Cassoni et al. specifically teach that there is an, "inhibitory effect of OT [oxytocin] and OT [oxytocin] analogues on the proliferation of human breast carcinoma cells", (please see again column 2, 4th paragraph, page 471). Furthermore, the direction and data provided by Cassoni et al. clearly teach that oxytocin and its analogues are effective in treating the proliferation of human breast carcinoma cells.

7. Next, applicant alleges that the rejection under 35 U.S.C. 103(a) as being unpatentable over Harris et al. in view of Boer et al. and further in view of Leckman et al. This rejection was found persuasive regarding the reference of Boer et al. Accordingly, this rejection has been modified to a rejection under 35 U.S.C. 103(a) as being unpatentable over Harris et al. in view of Leckman et al. Applicant argues that Leckman et al. fail to teach or suggest the administration of oxytocin to successfully alleviate an obsessive-compulsive disorder in a mammalian subject. In fact, applicant purports that Leckman et al. teach away from the instant invention by allegedly concluding that, "a role for oxytocin in the pathogenesis of obsessive compulsive disorder is meager and has mostly focused on systemically administered oxytocin's equivocal value as a therapeutic agent." This allegation was quoted to show the state of the art from a previously written article, such as Ansseau et al., (see page 734).

8. Leckman et al. do in fact teach that there is, "the emerging role of central OT [oxytocin] in a range of cognitive, grooming, affiliative, and sexual behaviors and how these behaviors are disrupted in some forms of OCD", (see page 735). Leckman et al.

also teach that, "there is a considerable body of evidence that OT [oxytocin] is a stress hormone and may serve as an endogenous anxiolytic. ", (see page 736). In fact, Leckman et al. teach that oxytocin can be an anxiolytic agent, because it acted similarly to diazepam; oxytocin acts as an antidepressant; oxytocin elevates pain thresholds and accordingly induces strong analgesia in man with intractable pain, (see page 737). For these reasons, Leckman et al. provides the skilled artisan with the motivation to use oxytocin to treat "anxiety disorders . . . [such as] OCD", (see page 737). In addition, the skilled artisan would have been motivated to employ oxytocin and its related derivatives to treat psychosis, such as OCD. Furthermore, the skilled artisan is provided with the teaching that patients with oxytocin-related OCD may be more responsive to serotonin reuptake inhibitors, (see Leckman et al., page 739). In fact, Leckman et al. specifically teach of a study where virtually all patients with OCD, "responded well to 5-HT reuptake inhibitors", (as cited from page 739). For these reasons, it would have been obvious to the skilled artisan to combine a serotonin reuptake inhibitor along with the administration of oxytocin and its analogues, which include carbetocin. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . .[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

9. Applicant also argues that in the rejection of claims 26-37 under 35 U.S.C. 103(a) as being unpatentable over Harris et al., the prior art reference of Harris et al. fails to

teach or suggest the efficacy of carbetocin or another oxytocin analog for prophylaxis or treatment of breast cancer or a psychiatric disorder in a mammalian patient. Claims 26-37 ??? are composition claims which include an intended use of this known prior art composition. Harris et al. do teach of inter alia, the nasal administration of the preferred pharmaceutical composition containing carbetocin as well as other analogs of oxytocin, (see column 2, lines 47-55). In response to applicant's argument that Harris et al. does not teach of the claimed intended use, which is intended to be used for the prophylaxis or treatment of breast cancer or a psychiatric disorder in a mammalian patient, the following is noted. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). For these reasons, the selection of a known material based on its suitability for its intended use, for example psychiatric disorder or breast cancer, supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 US 327, 65 USPQ 297 (1945).

The prior art rejection of claims 11, 12, 32, 49 and 50 under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Cassoni et al. in further view of Lipton et al. has been withdrawn and modified to reject claims 11, 12, 32, 49 and 50 under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S.

Patent No. 5,482,931 in view of Cassoni et al. in further view of and Windholz, Ed. of The Merck Index, 10th Edition, see the section entitled, *Claim Rejections - 35 USC § 103.*

Information Disclosure Statement

10. It is requested that a supplemental list be provided for the information disclosure statement filed on April 1, 2002 so that all of these references may be properly indicated as being considered.

Claim Rejections - 35 USC § 112

11. The rejection of claims 1-12 and 26-33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of breast cancer, does not reasonably provide enablement for the prevention or prophylaxis of breast cancer is maintained for the above-stated, reasons of record and the following detailed explanation.

12. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples;

and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to the prevention of breast cancer in mammalian patients. The method comprises administering carbetocin and other long-acting oxytocin analogues in a pharmaceutically acceptable carrier sufficient to inhibit growth of breast cancer in a mammalian patient.

(2) The state of the prior art

The compounds of the inventions are carbetocin. However, the prior art, such as Stein, teaches that cancer therapy is not only highly unpredictable but that there is no one example existing for efficacy of a single product against tumors generally

(3) The relative skill of those in the art

The relative skill of those in the art of anticancer pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often

react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art0; In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of carbetocin prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claims 1 and 26 are directed to the treatment as well as the prevention of breast cancer in mammalian patients with the administration of carbetocin and other long-acting oxytocin analogues. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed.

Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of carbetocin and other long-acting oxytocin analogues to be effective in treating not to mention the prevention of breast cancer is insufficient for enablement. The specification provides no guidance, in the way of

enablement for carbetocin and other long-acting oxytocin analogues for the prophylaxis of breast cancer in all mammalian patients other than in the mammals of rats. The specification provides no guidance, in the way written description for carbetocin and other long-acting oxytocin analogues for the prevention or the prophylaxis of breast cancer in all mammalian patients other than in the mammals of rats. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Accordingly, this is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses carbetocin and other long-acting oxytocin analogues that have the prophylaxis of breast cancer in all mammalian patients other than in the mammals of rats. However, the instant specification only has enablement for the treatment of breast cancer in mammals and the prophylaxis of breast cancer in the mammalian patients of rats.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine how the carbetocin and other long-acting oxytocin analogues would be enabled in this specification the prophylaxis of breast cancer in all mammalian patients other than in the mammals of rats, in particular humans.

13. Claims 13-25 and 34-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the psychiatric disorder of obsessive-compulsive disorder (OCD) in a mammalian patient, does not reasonably provide enablement for the treatment of other psychiatric disorders nor does the instant specification provide enablement for the prophylaxis of OCD, including any other psychiatric disorders, in a mammalian patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

14. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to using treating as well as the prophylaxis of psychiatric disorders with the administration of carbetocin and other long-acting oxytocin

analogues. The method comprises administering carbetocin and other long-acting oxytocin analogues for treating as well as the prophylaxis of psychiatric disorders.

(2) The state of the prior art

The compounds of the inventions are carbetocin and other long-acting oxytocin analogues

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21

USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art0; In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of carbetocin and other long-acting oxytocin analogues for the prophylaxis of OCD and other psychiatric disorders prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claims 13 and 34 are directed to the treatment as well as the prevention of a psychiatric disorder in mammalian patients with the administration of carbetocin and other long-acting oxytocin analogues. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of carbetocin and other long-acting oxytocin analogues to be effective in treating psychiatric disorders other than OCD as well as preventing OCD and other types of psychiatric disorders is insufficient for enablement. The specification provides no guidance, in the way of enablement for carbetocin and other long-acting oxytocin analogues for treating psychiatric disorders other than OCD as well as preventing OCD and other types of psychiatric disorders. In addition, the specification does not provide any enablement of derivatives or analogues of carbetocin or long-acting oxytocin that could be employed in this invention other than using carbetocin and only for treating the psychiatric disorder of OCD. In re Fisher, 427 F.2d

833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses carbetocin and other long-acting oxytocin analogues that have are used to treat and provide a prophylaxis for the all psychiatric disorders, including OCD. However, the instant specification only has enablement for using carbetocin for the treatment of OCD.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the analogues and derivatives of carbetocin and other long-acting oxytocin analogues for the treatment of psychiatric disorders other than OCD and the prophylaxis of all psychiatric disorders that would be enabled in this specification.

Claim Rejections - 35 USC § 103

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. Claims 1-12, 26-33 and 39-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Cassoni et al. Harris et al. teach of inter alia, the nasal administration of the preferred pharmaceutical composition containing carbetocin as well as other analogs of oxytocin, (see column 2,

lines 47-55). Harris et al. expands on this nasal composition of carbetocin by providing motivation to use the nasal composition for the management of diseases and abnormal conditions, (cited from column 3, lines 25-29). In addition, Harris et al. teach of adding the pharmaceutically acceptable excipients that contain citrate and/ or phosphate as well as sodium ions, (see column 2, lines 55-67). Harris et al. also teach of the preferred aspect of including at least one mucosal absorption enhancer, (see column 3, lines 13-16). Cassoni et al. disclose of the administration of oxytocin as well as oxytocin analogues, which show receptor-mediated inhibitory effects on the proliferation of human breast carcinoma cells. Accordingly, Cassoni et al. clearly provide the skilled artisan with the motivation to treat breast cancer with oxytocin and its analogues, (see page 471, column 2, 4th paragraph). Clearly, the prior art reference of Cassoni et al. provide the motivation necessary for the treatment of breast cancer with oxytocin and its analogues, (see page 471, column 2, 4th paragraph). The skilled artisan would have been motivated to utilize the preferred pharmaceutical peptide of carbetocin, as taught by Harris et al., as a treatment of breast cancer due to the fact that carbetocin is a structural analogue of oxytocin, (see column 2, lines 47-55 of Harris et al.) when the prior art reference of Harris et al. is combined with the teachings of Cassoni et al. Also, the determination of a dosage, mode of administration, addition or removal of pharmaceutically acceptable excipients, salts, diluents and adjuvants that have the optimum therapeutic index is well within the level of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum

pharmaceutically acceptable excipients and adjuvants in order to get the maximum effect of the active agent.

17. Claims 13-25 and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Leckman et al. Harris et al. teach of inter alia, the nasal administration of the preferred pharmaceutical composition containing carbetocin as well as other analogs of oxytocin, (see column 2, lines 47-55). Harris et al. expands on this nasal composition of carbetocin by providing motivation to use the nasal composition for the management of diseases and abnormal conditions, (cited from column 3, lines 25-29). In addition, Harris et al. teach of adding the pharmaceutically acceptable excipients that contain citrate and/ or phosphate as well as sodium ions, (see column 2, lines 55-67). Harris et al. also teach of the preferred aspect of including at least one mucosal absorption enhancer, (see column 3, lines 13-16). Leckman et al. teach of administering oxytocin to treat obsessive compulsive disorder, (see abstract and pages 723 and 724). Due to the fact that the prior art reference of Harris et al. specifically disclose of using oxytocin and its derivatives, namely carbetocin, to treat diseases and abnormal conditions, the skilled artisan would have been motivated to employ oxytocin and its derivatives, namely carbetocin, to treat diseases and abnormal conditions of obsessive compulsive disorder.

18. Leckman et al. do in fact teach that there is, "the emerging role of central OT [oxytocin] in a range of cognitive, grooming, affiliative, and sexual behaviors and how these behaviors are disrupted in some forms of OCD", (see page 735). Leckman et al. also teach that, "there is a considerable body of evidence that OT [oxytocin] is a stress

hormone and may serve as an endogenous anxiolytic. ", (see page 736). In fact, Leckman et al. teach that oxytocin can be an anxiolytic agent, because it acted similarly to diazepam; oxytocin acts as an antidepressant; oxytocin elevates pain thresholds and accordingly induces strong analgesia in man with intractable pain, (see page 737). For these reasons, Leckman et al. provides the skilled artisan with the motivation to use oxytocin to treat "anxiety disorders . . . [such as] OCD", (see page 737). In addition, the skilled artisan would have been motivated to employ oxytocin and its related derivatives to treat psychosis, such as OCD. Furthermore, the skilled artisan is provided with the teaching that patients with oxytocin-related OCD may be more responsive to serotonin reuptake inhibitors, (see Leckman et al., page 739). In fact, Leckman et al. specifically teach of a study where virtually all patients with OCD, "responded well to 5-HT reuptake inhibitors", (as cited from page 739). For these reasons, it would have been obvious to the skilled artisan to combine a serotonin reuptake inhibitor along with the administration of oxytocin and its analogues, which include carbetocin. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . .[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

19. Claims 26-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931. Harris et al. teach of inter alia, the nasal administration of the preferred pharmaceutical composition containing carbetocin as

well as other analogs of oxytocin, (see column 2, lines 47-55). Harris et al. expands on this nasal composition of carbetocin by providing motivation to use the nasal composition for the management of diseases and abnormal conditions, (cited from column 3, lines 25-29). In addition, Harris et al. teach of adding the pharmaceutically acceptable excipients that contain citrate and/ or phosphate as well as sodium ions, (see column 2, lines 55-67). Harris et al. also teach of the preferred aspect of including at least one mucosal absorption enhancer, (see column 3, lines 13-16). Also, the determination of a dosage, mode of administration, addition or removal of pharmaceutically acceptable excipients, salts, diluents and adjuvants that have the optimum therapeutic index is well within the level of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum pharmaceutically acceptable excipients and adjuvants in order to get the maximum effect of the active agent. Moreover, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). For these reasons, the selection of a known material based on its suitability for its intended use, for example psychiatric disorder or breast cancer, supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 US 327, 65 USPQ 297 (1945).

20. Claims 11, 12, 32, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. of U.S. Patent No. 5,482,931 in view of Cassoni et al. and Windholz, Ed. of The Merck Index, 10th Edition. Harris et al. teach of inter alia, the nasal administration of the preferred pharmaceutical composition containing carbetocin as well as other analogs of oxytocin, (see column 2, lines 47-55). Harris et al. expands on this nasal composition of carbetocin by providing motivation to use the nasal composition for the management of diseases and abnormal conditions, (cited from column 3, lines 25-29). In addition, Harris et al. teach of adding the pharmaceutically acceptable excipients that contain citrate and/ or phosphate as well as sodium ions, (see column 2, lines 55-67). Harris et al. also teach of the preferred aspect of including at least one mucosal absorption enhancer, (see column 3, lines 13-16). Cassoni et al. disclose of the administration of oxytocin as well as oxytocin analogues, which show receptor-mediated inhibitory effects on the proliferation of human breast carcinoma cells. Accordingly, Cassoni et al. clearly provide the skilled artisan with the motivation to treat breast cancer with oxytocin and its analogues, (see page 471, column 2, 4th paragraph). Windholz, Ed. of The Merck Index, 10th Edition disclose of the well-known pharmaceutical of tamoxifen to treat breast cancer, (see Compound No. 8923 on page 1300). "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . .[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Also, the determination of a dosage, mode

of administration, addition or removal of pharmaceutically acceptable excipients, salts, diluents and adjuvants that have the optimum therapeutic index is well within the level of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum pharmaceutically acceptable excipients and adjuvants in order to get the maximum effect of the active agent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (703) 308-4634. The examiner can normally be reached on Mondays through Fridays from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

DWAYNE C. JONES
PRIMARY EXAMINER

Tech. Ctr. 1614
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